DETAILED ACTION

Election/Restrictions

The election restriction mailed on 12/3/08 inadvertently indicated that claim 1 was a linking claim that links inventions II and III instead of placing the claim 1 in group I. Claim 1 recites a medicament comprising 'somatostatin or one of its agonist analogues' and hence belongs to group I invention. Also, claims 1, 12, 13, 16 and 17 are independent claims drawn to patentably distinct methods. Applicant's representative Mr. Vockrodt was contacted on 2/25/09 to inform him of the inadvertent inaccuracy in grouping claims. Mr. Vockrodt was informed that claim 1 will be placed in group I and the changes to election/restriction will be made apparent in the non-final office action on merit to which Mr. Vockrodt agreed to. Accordingly, the instant application is subjected to the following election/restriction as required under 35 USC 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I, claim(s) 1-11 and 18, drawn to method of regulating an ovarian follicular reserves comprising administering to a patient a medicament comprising somatostatin or one of its agonist analogs.

Group II, claim(s) 12, drawn to a method of determining the presence or absence of an effect of acceleration of follicle growth by conducting a toxicology test with a somatostatin or one of its agonist analog .....

Group III, claim(s) 13-15 and 19-21 drawn to a method of accelerating the start of growth of quiescent follicle in non-menopausal women.

Group IV, claim(s) 16, drawn to a method of supporting in vitro follicle development employing a somatostatin antagonist.

Group V, claim(s) 17, drawn to a method of determining the presence or absence of an effect of slowing of follicle growth comprising conducting a toxicology test with a somatostatin antagonist .....

The invention groups I-V lacks unity of invention as illustrated in the election/restriction mailed on 12/3/08.

Applicant's election with traverse of group III invention (claims 13-15 and 19-21) and election of

$$A^1\text{-cyclo}\{D\text{-}Cys\text{-}A^2\text{-}D\text{-}Trp\text{-}A^3\text{-}A^4\text{-}Cys\}\text{-}A^5\text{-}Y^1$$

(III)

in which:

$$A^1 = Cpa,\ A^2 = Pal,\ A^3 = Lys,\ A^4 = Thr,\ A^5 = Nal,\ Y^1 = NH_2$$

as species in the reply filed on 1/5/09 is acknowledged.

1. The traversal is on the ground(s) that the applicants argue that contrary to office's assertion that the special technical feature of group I is not "administering to a patient a medicament comprising somatostatin or one of its analogues" but rather "it is the use of somatostatin or its analogues in preparing a medicament for the regulation of (diminishment or acceleration) of the start of growth of follicles in quiescent stage". Applicants further assert that the cited reference of Weckbecker refers to a combination of compound of somatostatin class and a rapamycin macrolide for the prevention and treatment of cell proliferation. Applicants further state that instant invention is not directed to medicaments comprising combinations of somatostatin, a somatostatin agonist analogue, or a somatostatin antagonist analogue with a compound of another class nor the

use of the medicament of the invention for the prevention or treatment of cell hyperproliferation.

This is not found persuasive because the special technical feature of group I (as applicants states above) is the "the use of somatostatin or its analogues in preparing a medicament for the regulation of (diminishment or acceleration) of the start of growth of follicles in quiescent stage". Applicant's traversal arguments clearly illustrates that the medicament is for the intended purpose of regulation of the start of growth of follicles in the quiescent stage. Also, it should be noted that applicant's claims are drawn with the transitional phrase "comprising". Weckbecker discloses a composition of somatostatin and rapamycin and administration of the same to patients. Although, the administration of the composition is for a purpose other than the one recited in the instant invention, the requirement for the special technical feature of the instant invention is met in Weckbecker. The use of the transitional phrase "comprising" in the instant claims does not preclude other agents and components being present in the composition.

2. Applicants further argue that the International searching authority (ISA) did not find that the original claims as filed lacked unity of invention. This is not found persuasive because, statements made by the International Searching Authority or International Preliminary Examining Authority are not controlling in applications filed in the national phase. The MPEP states "The examiner may adopt any portion or all of the report on patentability of the IPEA or ISA upon consideration in the national stage so long as it is consistent with U.S. practice. The first Office action on the merits should indicate the report on patentability of the IPEA or ISA has been considered by the

examiner. The indication may be a mere acknowledgement." See MPEP 1893.03(e). Further, unity of invention is specifically authorized under 37 CFR 1.499. The MPEP states that "Examiners are reminded that unity of invention **>(not restriction practice pursuant to 37 CFR 1.141 -1.146)< is applicable in international applications (both Chapter I and II) **and** in national stage applications submitted under 35 U.S.C. 371." Thus, the mere fact that the International Searching Authority did not raise a lack of unity is not basis to prevent a lack of unity from being raised in the national application.

Hence the requirement is still deemed proper and is therefore made FINAL.

Status of the claims

Claims 1-21 are pending.

Claims 1-12 and 16-18 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking-claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/5/09.

Claims 19-21 have been added as new claims.

Claims 13-15 and 19-21 are examined on the merit.

A search for prior art indicated that the elected species is not free of prior art and has been used in the rejections as set forth below.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(a-d) is acknowledged. However, Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(a-d) as follows:

The foreign priority document submitted is not in English language. A translation of the same is required to grant the priority. The filing date of the priority document is not perfected unless applicant has filed a certified priority document in the application (and an English language translation, if the document is not in English) (see 37 CFR 1.55(a)(3)).

Specification

Abstract

The abstract of the disclosure is objected to because the abstract submitted is the first page of the WO 2005/034989 (i.e., the published PCT/FR04/002536). Hence, this application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. Correction is required. See MPEP § 608.01(b).

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

The instant specification cites number of patent and non-patent literature references throughout the disclosure. However, the IDS submitted on 7/24/06 list only four foreign patents (WO documents) and five non-patent literature references. The reference DeVet, et al., 2000, listed in the IDS. Applicants have not furnished a copy of the article in English, and hence the reference of De Vet, et al., **has not been considered.**

Arrangement of the Specification

The specification of the instant application also lacks the required format for presentation as provided in 37 CFR 1.77(b). The instant specification does not conform to the guidelines with sections under different titles such as:

(b) Cross-reference to related applications,

(f) Background of the invention.

(1) Field of the invention.

(2) Description of related art including information disclosed under 37 CFR 1.97 and 1.98.

(g) Brief summary of the invention, etc.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Objections

1. Claim 14 is objected to because of the following informalities:

Claim 14 recite a limitation "each aromatic α-amino acid being optionally substituted with one or more substituents independently includes a halogen atom, NO_2, OH, CN, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, (C_{1-6})alkoxy, Bzl, O-Bzt or NR^9R^{10}, R^9 and R^{10} are each independently H, O, or (C_{1-6})alkyl".

A proper way to recite the limitation would be "each aromatic α-amino acid being optionally substituted with one or more substituents, wherein each of the substituents independently selected from ~~includes~~ the group of halogen atom, NO_2, OH, CN, (C_{1-}

$_{6}$)alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, (C_{1-6})alkoxy, Bzl, O-Bzt or NR^9R^{10}, R^9 and R^{10} are each independently H, O, or (C_{1-6})alkyl"

2. Claim 14 is objected to because of the following informalities:

Claim 14 recite a limitation, "each nitrogen atom with a peptide amide bond and the amino group of A^1 are optionally substituted with a methyl group".

A proper way to recite the limitation would be "each nitrogen atom ~~with~~ of a peptide amide bond and the amino group of A^1 are optionally substituted with a methyl group"

3. Claim 15 is objected to because of the following informalities:

Claim recites a character " ❖ " that is not recognized in the art.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 13-15 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13-15 and 19-21 recite the term "analogues" in context of somatostatin antagonist. The specification provides a very broad definition to describe the structural

aspects of somatostatin antagonist analogues as "[T]he somatostatin antagonist analogue can be a cyclic or non cyclic polypeptide, a fusion or recombination protein, a non-peptide chemical entity (i.e. a peptidomimetic) or also a "SS-like" peptide such as corticostatin". The definition include functional language such as "[T]he antagonist analogues to be used must have a high affinity for the SST receptor and inhibit the functional activity of SST14 or SST28 such as the inhibition of the secretion of growth hormone by somatotrope cells of the pituitary and/or the inhibition of the in vitro proliferation of pituitary adenoma cells. Preferably, the somatostatin antagonist analogue has a high affinity for all or at least 2 or 3 of the sub-types of SST receptors or a greater affinity for at least one of the sub-types 1, 2, 3, 4 and 5 (for example for sub-type 2)".

Hence, it is unclear form the claim as recited and the definition as provided in the specification the true structural characteristics of these somatostatin antagonist analogs. According to the definition for 'analog' as provided by International Union of Pure and Applied Chemistry (IUPAC), in Wermuth, Pure and Appl. Chem, 1998, 70, 1129-1143, "an analog is a drug whose structure is related to that of another drug but whose chemical and biological properties may be quite different" (Page 1131). Therefore, the disclosure of proper chemical structure for the analogs that correlates with the desired biological function is essential. Hence the claims are being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claims 14, 15 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14, 15 and 19-21 recite a term "includes" in defining the somatostatin antagonist analog. It is unclear form the claim as recited 'what else?' is included in the somatostatin antagonist analog apart from the recited peptides of formula III in claim 14. In claims 15 the limitation recites "somatostatin antagonist analog includes the following peptides" and recites not only peptides, it recites non-peptidic compounds with code names such as BN-81674 and SRA-880. It is unclear how many peptides are included in the somatostatin antagonist analog. In claims 19-21, it is unclear form the claim as recited 'what else' is included in the somatostatin antagonist analog apart from the recited peptide. The claims as recited with the term "includes" does not clearly define the 'metes and bounds' of the recited claims and hence are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

3. Claims 14 and 15 recites the limitation "combinations thereof" in at the end of the claim recitation. There is insufficient antecedent basis for this limitation in the claim. The claim 13 form which claims 14 and 15 depends from is drawn to "**a** somatostatin antagonist analog". Hence claims14 and 15 lacks antecedent basis in the base claim 13.

4. Claims 14 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The variable 'R' in 'OR' as recited as a variable for the moiety 'Y^1' in the formula III is not defined in the claim as recited. Hence claims 14 and 19-21 are

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 13 is drawn to a method of accelerating the start of growth of quiescent follicles in non-menopausal women comprising administering to a patient a medicament comprising a somatostatin antagonist analogue.

Claim as recited defines the somatostatin antagonist analog by only function. Claim as presented is interpreted as being drawn to any and all known and unknown analogs of somatostatin antagonist.

Factors to be considered in making the determination as to whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing include:

a. Actual reduction to practice;
b. Disclosure of drawings or structural chemical formulas;
c. Sufficient relevant identifying characteristics such as:
    i. Complete structure,
    ii. Partial structure,
    iii. Physical and/or chemical properties or

iv. Functional characteristics when coupled with a known or disclosed correlation between function and structure;

d. Method of making the claimed invention;
e. Level of skill and knowledge in the art and
f. Predictability in the art.

While all of these factors are considered, a sufficient number for a *prima facie* case are discussed below.

Claim 13 as recited does not recite a complete or partial structure or a chemical formula to provide adequate written description to the claims. The specification as disclosed provides a very broad definition to describe the structural aspects of somatostatin antagonist analog as "[T]he somatostatin antagonist analogue can be a cyclic or non cyclic polypeptide, a fusion or recombination protein, a non-peptide chemical entity (i.e. a peptidomimetic) or also a "SS-like" peptide such as corticostatin". The definition also include functional language such as "[T]he antagonist analogues to be used must have a high affinity for the SST receptor and inhibit the functional activity of SST14 or SST28 such as the inhibition of the secretion of growth hormone by somatotrope cells of the pituitary and/or the inhibition of the in vitro proliferation of pituitary adenoma cells. Preferably, the somatostatin antagonist analogue has a high affinity for all or at least 2 or 3 of the sub-types of SST receptors or a greater affinity for at least one of the sub-types 1, 2, 3, 4 and 5 (for example for sub-type 2)".

The prior art recognizes the somatostatin antagonists as being represented by different classes of compounds such as cyclic peptides (Hepplemann, 1999, Neurosciences letters, 259, 62-64 and WO 02/072602 of Coy), arginine, a simple amino acid (Terzolo, 2000, The Journal of Clinical Endocrinology and Metabolism, 85, 1310-1315), a linear hexapeptide (Baumbach, 1998, Molecular Pharmacology, 54, 864-873), and non-peptide molecules (Poitout, 2001, J. Med. Chem., 44, 2990-3000), etc. Although,

the prior art recognizes different classes of compounds as somatostatin antagonist, the definition for 'analog' provided by International Union of Pure and Applied Chemistry (IUPAC), in Wermuth, Pure and Appl. Chem, 1998, 70, 1129-1143, as "[A]n analog is a drug whose structure is related to that of another drug but whose chemical and biological properties may be quite different" (Page 1131) implies that disclosure of complete or partial structure of a molecule is essential to provide support to the desired function correlated to the structure. Therefore, the disclosure of the chemical structure for the analogs that correlates with the desired biological function is essential to provide adequate written description in the instant case.

The instant specification discloses one somatostatin antagonist peptide in example 3 to practice the method recited in the claim. Therefore, the disclosure as originally filed does not adequately support the claims as recited commensurate with the scope of the claims as presented. Therefore, the claim as recited lacks written description and one of ordinary skill in the art would find it difficult practice the instant method as claimed commensurate with the scope of the claims.

Therefore, claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Terzolo, 2000, The Journal of Clinical Endocrinology and Metabolism, 85, 1310-1315.

Claim 13 is drawn to a method of accelerating the start of growth of quiescent follicles in non-menopausal women comprising administering to a patient a medicament comprising a somatostatin antagonist analogue.

Claim as presented is interpreted as being drawn to any and all known and unknown analogs of somatostatin antagonist analogs that exhibits the desired function of accelerating the start of growth of quiescent follicles in non-menopausal women.

Terzolo discloses that they studied the growth hormone (GH) responses to growth hormone releasing hormone (GHRH) alone or in combination with arginine (title). Terzolo discloses that arginine (a functional somatostatin antagonist) was infused into 10 patients of 'Adrenal Incidentaloma' and 13 control subjects (abstract and 'Methods' section on page 1311). Terzolo discloses that pre-menopausal women were studied in the early follicular phase of the menstrual cycle (page 1312, column 1, paragraph 2). From table 1, it should be noted that 3 of the 13 control patients are women (ages 32, 34 and 44) who are normal healthy individuals are in the age group below 44 years and hence constitute the patient population of 'non-menopausal women' recited in the instant claim. Administration of arginine, a functional somatostatin antagonist to the above mentioned women meets the method steps of the instant claim 13. Since somatostatin antagonist (arginine in this case) was administered to the desired patient population (non-menopausal women), it is inherent that it would result in accelerating the start of growth

of quiescent follicles as recited in the instant claim. MPEP section 2112 states that, "[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."

Hence, Terzolo anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13-15 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terzolo, 2000, The Journal of Clinical Endocrinology and Metabolism, 85, 1310-1315 in view of Coy (WO 02/072602).

Claims are drawn to a method of accelerating the start of growth of quiescent follicles in non-menopausal women comprising administering to a patient a medicament comprising a somatostatin antagonist analogue.

Terzolo discloses that they studied the growth hormone (GH) responses to growth hormone releasing hormone (GHRH) alone or in combination with arginine (title). Terzolo discloses that arginine (a functional somatostatin antagonist) was infused into 10 patients of 'Adrenal Incidentaloma' and 13 control subjects (abstract and 'Methods' section on page 1311). Terzolo also discloses that pre-menopausal women were studied in the early follicular phase of the menstrual cycle (page 1312, column 1, paragraph 2). From table 1, it should be noted that 3 of the 13 control patients who are normal healthy women are in the age group below 44 years and hence constitute the patient population of 'non-menopausal women' recited in the instant claim. Administration of arginine, a functional somatostatin antagonist to the above mentioned desired women population meets the method steps of the instant claim 13.

Terzolo does not disclose the elected species of the instant invention, i.e., the cyclic peptide represented by the formula III:

$$A^1\text{-cyclo}\{\text{D-Cys-}A^2\text{-D-Trp-}A^3\text{-}A^4\text{-Cys}\}\text{-}A^5\text{-}Y^1$$

(III)

in which:

$$A^1 = \text{Cpa},\ A^2 = \text{Pal},\ A^3 = \text{Lys},\ A^4 = \text{Thr},\ A^5 = \text{Nal},\ Y^1 = NH_2$$

in which the various variables are defined as shown above.

The instant claims are being examined to the extent that they read on the elected species in claims 14, 15 and 19-21. It should be noted that applicants election of A^2=Pal,

reads on the species comprising 2-Pal, 3-Pal and 4-Pal and likewise A^5=Nal reads on 2-Nal.

Coy discloses the instant generic formula III (with the variable defined in an identical manner) on page 3 and on page 30 (as generic formula I in Coy). On page 4 of Coy, the species corresponding to the elected species are disclosed as shown below:

NmeCpa-cyclo(DCys-3-Pal-DTrp-Lys-Thr-Cys)-2-Nal-NH_2;
Cpa-cyclo(NMeDCys-3-Pal-DTrp-Lys-Thr-Cys)-2-Nal-NHMe;
Cpa-cyclo(DCys-NMe3-Pal-DTrp-Lys-Thr-Cys)-2-Nal-NH_2;
Cpa-cyclo(DCys-3-Pal-NMeDTrp-Lys-Thr-Cys)-2-Nal-NH_2;
Cpa-cyclo(DCys-3-Pal-DTrp-NMeLys-Thr-Cys)-2-Nal-NH_2;
Cpa-cyclo(DCys-3-Pal-DTrp-Lys-NMeThr-Cys)-2-Nal-NH_2;
Cpa-cyclo(DCys-3-Pal-DTrp-Lys-Thr-NMeCys)-2-Nal-NH_2;
Cpa-cyclo(DCys-3-Pal-DTrp-Lys-Thr-Cys)-Nme2-Nal-NH_2;

The above species and the generic formula I (on page 3 and on page 30) of Coy reads on the elected species of the instant invention. Coy also discloses that the peptides of the invention is useful in treating disease or disorders associated with the need to promote the release of growth hormone (GH) (page 9, lines 22-24). Claim 13 (page 33) of Coy is drawn to a method of promoting the release of growth hormone (GH) in a human which comprises administration of effective amounts of peptides of invention.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Terzolo and Coy to arrive at the instant invention, because both Terzolo and Coy teaches administration of somatostatin antagonists (arginine in Terzolo and peptides of instant invention in Coy) for the same purpose of release of growth hormone in patients. Instant invention is drawn to method of accelerating the start of the growth of

quiescent follicle cells in non-menopausal women. As illustrated above, Terzolo administers arginine, a functional somatostatin antagonist to non-menopausal women which acts on the release of growth hormone and hence accelerates the growth of quiescent follicles. Hence, one of ordinary skill in the art would have been motivated to administer the elected cyclic peptide of the instant invention as functional equivalent of arginine (a known somatostatin antagonist) into non-menopausal women for the aforementioned purpose for the release of growth hormone that accelerates the growth of quiescent follicles in non-menopausal women as shown by Terzolo.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654